

## PATENT COOPERATION TREATY

## PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY  
(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

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Applicant's or agent's file reference 13751-019WO1	FOR FURTHER ACTION		See Form PCT/IPEA/416
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International Patent Classification (IPC) or national classification and IPC IPC(7): C12 N 05/10, 15/85, 15/87 and US Cl.: 435/320.1, 325, 462			
Applicant BIOGEN IDEC MA INC.			
<p>1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of <u>5</u> sheets, including this cover sheet.</p> <p>3. This report is also accompanied by ANNEXES, comprising:</p> <p>a. <input type="checkbox"/> (sent to the applicant and to the International Bureau) a total of ___ sheets, as follows:</p> <p><input type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).</p> <p><input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.</p> <p>b. <input type="checkbox"/> (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) _____, containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).</p> <p>4. This report contains indications relating to the following items:</p> <p><input checked="" type="checkbox"/> Box No. I Basis of the report</p> <p><input type="checkbox"/> Box No. II Priority</p> <p><input checked="" type="checkbox"/> Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p><input type="checkbox"/> Box No. IV Lack of unity of invention</p> <p><input checked="" type="checkbox"/> Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p><input type="checkbox"/> Box No. VI Certain documents cited</p> <p><input type="checkbox"/> Box No. VII Certain defects in the international application</p> <p><input checked="" type="checkbox"/> Box No. VIII Certain observations on the international application</p>			
Date of submission of the demand 13 May 2005 (13.05.2005)		Date of completion of this report 24 June 2005 (24.06.2005)	
Name and mailing address of the IPEA/US Mail Stop PCT, Attn: IPEA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230		Authorized officer <i>Valerie Ball-Harris</i> Jennifer Dunston Telephone No. (571) 272-1600	

Form PCT/IPEA/409 (cover sheet)(January 2004)

# INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

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## Box No. I Basis of the report

1. With regard to the language, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.
  - ☐ This report is based on translations from the original language into the following language \_\_\_\_\_, which is the language of a translation furnished for the purposes of:
    - ☐ international search (under Rules 12.3 and 23.1(b))
    - ☐ publication of the international application (under Rule 12.4)
    - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)
2. With regard to the elements of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:
  - ☒ the international application as originally filed/furnished
  - ☒ the description:
    - pages 1-34 as originally filed/furnished
    - pages\* NONE received by this Authority on \_\_\_\_\_
    - pages\* NONE received by this Authority on \_\_\_\_\_
  - ☒ the claims:
    - pages 35-37 as originally filed/furnished
    - pages\* NONE as amended (together with any statement) under Article 19
    - pages\* NONE received by this Authority on \_\_\_\_\_
    - pages\* NONE received by this Authority on \_\_\_\_\_
  - ☒ the drawings:
    - pages 1/10-10/10 as originally filed/furnished
    - pages\* NONE received by this Authority on \_\_\_\_\_
    - pages\* NONE received by this Authority on \_\_\_\_\_
  - ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing.
3. ☐ The amendments have resulted in the cancellation of:
  - ☐ the description, pages \_\_\_\_\_
  - ☐ the claims, Nos. \_\_\_\_\_
  - ☐ the drawings, sheets/figs \_\_\_\_\_
  - ☐ the sequence listing (*specify*): \_\_\_\_\_
  - ☐ any table(s) related to the sequence listing (*specify*): \_\_\_\_\_
4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
  - ☐ the description, pages \_\_\_\_\_
  - ☐ the claims, Nos. \_\_\_\_\_
  - ☐ the drawings, sheets/figs \_\_\_\_\_
  - ☐ the sequence listing (*specify*): \_\_\_\_\_
  - ☐ any table(s) related to the sequence listing (*specify*): \_\_\_\_\_

\* If item 4 applies, some or all of those sheets may be marked "superseded."

# INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

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## Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application

☒ claims Nos. 3,7,9 and 10

because:

☐ the said international application, or the said claim Nos. \_\_\_\_\_ relate to the following subject matter which does not require an international preliminary examination (*specify*):

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. \_\_\_\_\_ are so unclear that no meaningful opinion could be formed (*specify*):

☒ the claims, or said claims Nos. 3,7,9 and 10 are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for said claims Nos. \_\_\_\_\_

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form

☐

has not been furnished

☐

does not comply with the standard

the computer readable form

☐

has not been furnished

☐

does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.

☐ See Supplemental Box for further details.

## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.  
PCT/US04/33868**Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement****1. Statement**

Novelty (N)	Claims <u>4-6</u>	YES
	Claims <u>1, 2, 8, 11-30</u>	NO
Inventive Step (IS)	Claims <u>NONE</u>	YES
	Claims <u>1, 2, 4-6, 8, 11-30</u>	NO
Industrial Applicability (IA)	Claims <u>1, 2, 4-6, 8, 11-30</u>	YES
	Claims <u>NONE</u>	NO

**2. Citations and Explanations (Rule 70.7)**

Claims 1, 2, 8 and 11-30 lack novelty under PCT Article 33(2) as being anticipated by Perkins et al. Perkins et al teach methods of using recombinase mediated recombination target gene expression vectors and/or genes for insertion into platform chromosomes as well as kits containing the combinations of vectors encoding a recombinase and integrase and primers for introduction of the site recognized thereby (e.g. paragraph [0013]). Perkins et al teach the use of the *Saccharomyces cerevisiae* 2 micron based FLP/FRT system where FRT sites are placed in vectors and the platform chromosome (e.g. paragraph [0179] and [0156]). The target gene expression vectors carry, for example, genes for gene therapy, genes for transgenic animal or plant production, and those required for cellular protein production of interest along with promoter sequences (e.g. paragraph [0189]). One of the promoters disclosed by Perkins et al is the CMV-IE promoter (e.g. Figure 8). Further, Perkins et al teach the use of the SV40 polyA signal sequence (e.g. paragraphs [0335] and [0421]). Perkins et al teach the use of the *dhfr* gene as a selectable marker (e.g. paragraphs [0239]-[0240]). Regarding the use of an intervening domain between the second promoter/enhancer region and the second polynucleotide of interest, Perkins et al disclose the presence of intervening plasmid backbone sequence between the chicken beta-actin promoter and the eGFP polynucleotide sequence, for example (Figure 10). Perkins et al teach the transfection of the targeting expression vectors into CHO DG44 cells (*dhfr*-) using serum-free medium and suspension culture (e.g. paragraphs [0222] and [0232]).

Claims 4-6 lack an inventive step under PCT Article 33(3) as being obvious over Perkins et al in view of Chapman et al. The teachings of Perkins et al are described above and applied as before except Perkins et al do not teach a recombination cassette that comprises intron A from human CMV immediate early 1 gene (hCMV IE1). Chapman et al teach the insertion of intron A from human cytomegalovirus immediate early gene (IE1) within coding sequences of interest to increase the expression of the polynucleotide into which it is inserted (e.g. Figure 3; Discussion). In view of this teaching, it would have been obvious to one of ordinary skill in this art to use the intron A of Chapman et al in the target gene expression vector of Perkins et al.

Claims 1, 2, 4-6, 8 and 11-30 meet the criteria set out in PCT Article 33(4), and thus have industrial applicability because the subject matter claimed can be made or used in industry.

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**Box No. VIII** Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

Claims 15-17, 19-21 and 25-27 are objected to under PCT Rule 66.2(a)(v) as lacking clarity under PCT Article 6 because claims 15-17, 19-21 and 25-27 indefinite for the following reason(s): claims 15-17, 19-21, 25 and 26 recite the phrase "adapted for" and claim 27 recites the phrase "derived from." The metes and bounds of these phrases are unclear. It is not clear to what extent the invention can be adapted or derived and still meet the claim limitations with regard to structure and/or function.